

04D0  
②

I hereby certify that this correspondence is being  
deposited with Federal Express as Fedex Express  
Saver in a box addressed to:  
Commissioner of Patents and Trademarks,  
U.S. Patent and Trademark Office, 2011 South Clark Place,  
Crystal Plaza 2, Room 1B03 - MAILROOM,  
Arlington, VA 22202  
on September 5, 2001  
Date of Deposit

Carolyn Roberts  
Name of applicant, assignee  
or Registered Representative  
  
Signature

  
September 5, 2001  
Date of Signature

Patent  
Case No. P-188

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Clark M. Whitehead et al. )  
Serial No.: 09/938,009 ) Examiner: Not Yet Assigned  
Filed: August 23, 2001 ) Art Unit: Not Yet Assigned  
For: METHODS FOR TREATMENT OF )  
LUPUS ERYTHEMATOSUS )

INFORMATION DISCLOSURE STATEMENT

Honorable Commissioner of  
Patents and Trademarks  
Washington, D.C. 20231

Sir:

Pursuant to the obligation under 37 C.F.R. § 1.56 and in conformance with 37 C.F.R. §§ 1.97-1.99, Applicants hereby submit the following documents for consideration by the Examiner. A copy of each has been enclosed along with two copies of the PTO-1449 form.

## U.S. Patents

<u>Patent No.</u>	<u>Date</u>	<u>Name</u>
3,031,450	April 24, 1962	Fischer et al.
3,161,654	December 15, 1964	Shen
3,312,730	April 4, 1967	Winter et al.
3,322,755	May 30, 1967	Roch et al.
3,325,358	June 13, 1967	Winter et al.
3,532,752	October 6, 1970	Shen
3,642,785	February 15, 1972	Shen et al.
3,647,858	March 7, 1972	Hinkley et al.
3,654,349	April 4, 1972	Shen et al.
3,692,651	September 19, 1972	Sletzinger et al.
3,692,825	September 19, 1972	Conn
3,737,455	June 5, 1973	Shen et al.
3,851,063	November 26, 1974	Shen et al.
3,860,636	January 14, 1975	Shen et al.
4,402,979	September 6, 1983	Shen et al.
4,307,114	December 22, 1981	Dvornik et al.
4,423,074	December 27, 1983	Dvornik et al.
4,423,075	December 27, 1983	Dvornik et al.
4,880,810	November 14, 1989	Lowe, III
4,885,301	December 5, 1989	Coates
5,298,525	March 29, 1994	Yoon et al.
5,401,774	March 28, 1995	Pamukcu et al.
5,470,873	November 28, 1995	Yoon
5,488,055	January 30, 1996	Kumar et al.
5,527,896	June 18, 1996	Wigler et al.
5,602,019	February 11, 1997	Beavo et al.
5,602,171	February 11, 1997	Tang et al.
5,614,530	March 25, 1997	Kumar et al.

<u>Patent No.</u>	<u>Date</u>	<u>Name</u>
5,614,627	March 25, 1997	Takase et al.
5,708,022	January 13, 1998	Bastos et al.
5,776,752	July 7, 1998	Beavo et al.
5,789,553	August 4, 1998	Beavo et al.
5,798,374	August 25, 1998	Tang et al.
5,800,987	September 1, 1998	Beavo et al.
5,852,035	December 22, 1998	Pamukcu et al.
5,858,694	January 12, 1999	Piazza et al.
5,861,396	January 19, 1999	Niewöhner et al.
5,874,440	February 23, 1999	Pamukcu et al.
5,883,110	March 16, 1999	Tang et al.
5,885,834	March 23, 1999	Epstein
5,902,827	May 11, 1999	Pamukcu et al.
5,922,595	July 13, 1999	Fisher et al.
5,942,520	August 24, 1999	Pamukcu et al.
5,948,911	September 7, 1999	Pamukcu et al.
5,958,982	September 28, 1999	Pamukcu et al.
5,990,117	November 23, 1999	Pamukcu et al.
5,998,463	December 7, 1999	Hulin et al.
6,008,215	December 28, 1999	Flockerzi
6,015,677	January 18, 2000	Beavo et al.
6,034,099	March 7, 2000	Pamukcu et al.
6,037,345	March 14, 2000	Pamukcu et al.
6,046,199	April 4, 2000	Pamukcu et al.
6,046,206	April 4, 2000	Pamukcu et al.
6,046,216	April 4, 2000	Piazza et al.
6,060,477	May 9, 2000	Piazza et al.
6,066,634	May 23, 2000	Sperl et al.
6,069,240	May 30, 2000	Wigler et al.
6,071,934	June 6, 2000	Sperl et al.

<u>Patent No.</u>	<u>Date</u>	<u>Name</u>
6,077,842	June 20, 2000	Pamukcu et al.
6,080,540	June 27, 2000	Wigler et al.
6,080,742	June 27, 2000	Germann et al.
6,080,772	June 27, 2000	Tang et al.
6,100,025	August 8, 2000	Wigler et al.
6,107,295	August 22, 2000	Rochus et al.
6,124,303	September 26, 2000	Pamukcu et al.
6,133,271	October 17, 2000	Pamukcu et al.
6,143,746	November 7, 2000	Daugan et al.
6,143,759	November 7, 2000	Flockerzi
6,143,765	November 7, 2000	Tang et al.
6,143,777	November 7, 2000	Jonas et al.
6,169,090	January 2, 2001	Dyke et al.
6,174,884	January 16, 2001	Haning et al.
6,187,779	February 13, 2001	Pamukcu et al.
6,200,771	March 13, 2001	Liu et al.
6,200,980	March 13, 2001	Piazza et al.
6,207,666	March 27, 2001	Piazza et al.
6,211,177	April 3, 2001	Sperl et al.
6,211,220	April 3, 2001	Pamukcu et al.
6,232,312	May 15, 2001	Pamukcu et al.
6,235,742	May 22, 2001	Bell et al.
6,235,776	May 22, 2001	Pamukcu et al.
6,235,782	May 22, 2001	Pamukcu et al.
6,239,136	May 29, 2001	Pamukcu et al.
6,251,904	June 26, 2001	Bunnage et al.
6,255,303	July 3, 2001	Sterk et al.
6,255,456	July 3, 2001	Fisher et al.
6,258,833	July 10, 2001	Martins et al.
6,268,372	July 31, 2000	Pamukcu et al.

### Foreign Patent Documents

<u>Document No.</u>	<u>Date</u>	<u>Country</u>
EP 0 293 063 B1	March 18, 1992	EPO
EP 0 347 146 B1	September 1, 1993	EPO
EP 0 349 239 A2	January 3, 1990	EPO
EP 0 352 960 B1	October 26, 1994	EPO
EP 0 351 058 B1	June 2, 1993	EPO
EP 0 395 328 A2	October 31, 1990	EPO
EP 0 428 268 A2	May 22, 1991	EPO
EP 0 463 756 A1	January 2, 1992	EPO
EP 0 526 004 A1	February 3, 1993	EPO
EP 0 722 943 A1	January 8, 1996	EPO
EP 0 722 944 A1	January 8, 1996	EPO
EP 1 074 258 A3	April 18, 2001	EPO
GB 807,826	January 21, 1959	United Kingdom
GB 2 063 249 A	June 3, 1981	United Kingdom
HEI 8-311035	November 26, 1996	Japan
SHO 61-106521	May 24, 1986	Japan
WO 01/04099 A1	January 18, 2001	PCT
WO 00/12501	March 9, 2000	PCT
WO 00/26201	May 11, 2000	PCT
WO 00/23091	April 27, 2000	PCT
WO 00/26208	May 11, 2000	PCT
WO 00/27861	May 18, 2000	PCT
WO 00/42017	July 20, 2000	PCT
WO 00/42018	July 20, 2000	PCT
WO 00/42019	July 20, 2000	PCT
WO 00/42034	July 20, 2000	PCT
WO 00/59890	October 12, 2000	PCT
WO 00/64424	November 2, 2000	PCT

<u>Document No.</u>	<u>Date</u>	<u>Country</u>
WO 99/65880	December 23, 1999	PCT
WO 98/19679A1	May 14, 1998	PCT (Claims Only)
WO 98/17668	April 30, 1998	PCT
WO 98/14448	April 9, 1998	PCT
WO 98/06722	February 19, 1998	PCT
WO 97/24334	July 10, 1997	PCT
WO 97/03985	February 6, 1997	PCT
WO 97/03675	February 6, 1997	PCT
WO 94/29277	December 22, 1994	PCT
WO 93/07149	April 15, 1993	PCT

### Other Art - Articles

Ahmad F. et al., IL-3 ad IL-4 Activate Cyclic Nucleotide Phosphodiesterases 3 (PDE3) and 4 (PDE4) by Different Mechanisms in FDCP2 Myeloid Cells, *J. Immunology* Vol. 162, Part 8, pp. 4864-4875 (Apr 15 1999).

Boven LA et al., Macrophage inflammatory protein-1 alpha (MIP-1alpha), MIP-1beta, and RANTES mRNA semiquantification and protein expression in active demyelinating multiple sclerosis (MS) lesions, *Clin. Exp. Immunol.* 2000 Nov.; 122(2): 257-63 (Abstract Only).

Cooper N. et al., A comparison of the inhibitory activity of PDE4 inhibitors on leukocyte PDE4 activity in vitro and eosinophil trafficking in vivo, *British Journal of Pharmacology* (1999) 126, pp. 1863-1871.

Czirjak L. et al., Investigation of the alveolar macrophages and T lymphocytes in 15 patients with systemic sclerosis, *Clin Rheumatology* 1999; 18(5), pp. 357-363 (Abstract Only).

Danahay H. et al., PDE4 inhibition and a corticosteroid in chronically antigen exposed conscious guinea-pigs, *Clinical and Experimental Allergy*, 1998, Vol. 28, pp. 513-522.

Duggan, D.E. et al., Identification of the Biologically Active Form of Sulindac, *J. Pharm. & Exper. Therap.*, Vol. 201, No. 1, pp.8-13 (1977).

Gantner F. et al., Characterization of the Phosphodiesterase (PDE) Pattern of in Vitro-Generated Human Dendritic Cells (DC) and the Influence of PDE Inhibitors on DC Function, *Pulmonary Pharmacology & Therapeutics* (1999) 12, pp. 377-386.

Gantner F. et al., In vitro differentiation of human monocytes to macrophages: change of PDE profile and its relationship to suppression of tumour necrosis factor- $\alpha$  release by PDE inhibitors,

British Journal of Pharmacology (1997) 121, pp. 221-231.

Gehrman J. et al., Amyloid precursor protein (APP) expression in multiple sclerosis lesions, *Glia* 1995 Oct;15(2), pp. 141-151 (Abstract Only).

Germain N. et al., Selective phosphodiesterase inhibitors modulate the activity of alveolar macrophages from sensitized guinea-pigs, *Eur. Respir. J.* 1998;12, pp. 1334-1339.

Giembycz, M.A., Phosphodiesterase 4 Inhibitors and the Treatment of Asthma, *Drugs* 2000 Feb; 59(2), pp. 193-212.

Gonzaga, R.A.F. et al., *The Lancet*, 3/30/85, p. 751.

Hammermann, R. et al., Phosphodiesterase Inhibitors and Forskolin Up-regulate Arginase Activity in Rabbit Alveolar Macrophages, *Pulmonary Pharmacology and Therapeutics* 2000; Vol. 13, No. 3, pp. 141-147.

He W. et al., Novel Cyclic Compounds as Potent Phosphodiesterase 4 Inhibitors, *J. Med. Chem.*, Vol. 41, Part 22, pp. 4216-4223 (Oct 22 1998).

Hollander AP et al., Expression of hypoxia-inducible factor 1 alpha by macrophages in the rheumatoid synovium: implications for targeting of therapeutic genes to the inflamed joint, *Arthritis Rheum.* 2001 Jul; 44(7): 1540-4 (Abstract Only).

Imahashi K. et al., Type IV Phosphodiesterase Inhibitor Suppresses Insulin-Dependent Myocardial Glucose Uptake, *Clin Exp Pharmacol Physiol* 2001 Apr;28(4), pp. 290-291 (Abstract Only)

Ishikawa O. et al., Macrophage infiltration in the skin of patients with systemic sclerosis, *J. Rheumatology* 1992 Aug; 19(8), pp. 1202-1206 (Abstract Only).

Kapur S. et al., Expression of Nitric Oxide Synthase in Skeletal Muscle, *Diabetes*, Vol. 46, Nov. 1997, pp. 1691-1700.

Kelly J. et al., Characterization of phosphodiesterase 4 in guinea-pig macrophages: multiple activities, association states and sensitivity to selective inhibitors, *British Journal of Pharmacology* (1998) 124, PP. 129-140.

Kelly J. et al., Phosphodiesterase 4 in macrophages: relationship between cAMP accumulation, suppression of cAMP hydrolysis and inhibition of [<sup>3</sup>H]R-(–)-rolipram binding by selective inhibitors, *Biochem. J.* (1996) 318, pp. 425-436.

Kumar A. et al., Analgesic and anti-inflammatory effects of phosphodiesterase inhibitors, *Indian J Exp Biol* 2000 Jan;38(1), pp. 26-30 (Abstract Only)

Lee MS et al., A comparative immunohistochemical study of lichen planus and discoid lupus erythematosus, *Australas Jj. Dermatol.* 1996 Nov.; 37(4): 188-92 (Abstract Only).

McPherson M.A. et al., A cyclic nucleotide PDE5 inhibitor corrects defective mucin secretion in submandibular cells containing antibody directed against the cystic fibrosis transmembrane conductance regulator protein, FEBS Letters 464 (1999), pp. 48-52.

Mery P.F. et al., Erythro-9-(2-hydroxy-3-nonyl)adenine inhibits cyclic GMP-stimulated phosphodiesterase in isolated cardiac myocytes, Mol. Pharmacology 1995 Jul;48(1), pp. 121-130 (Abstract Only)

Méry, Pierre-François et al., EHNA as an Inhibitor of PDE2: A Pharmacological and Biochemical Study in Cardiac Myocytes, Phosphodiesterase Inhibitors (1996), pp. 81-88.

Michie, A.M. et al., Rapid regulation of PDE-2 and PDE-4 cyclic AMP phosphodiesterase activity following ligation of the T cell antigen receptor on thymocytes: analysis using the selective inhibitors erythro-9-(2-hydroxy-3-nonyl)-adenine (EHNA) and rolipram, Cell Signal 1996 Feb;8(2), pp. 97-110.

Niebauer J. et al., Local L-Arginine Delivery After Balloon Angioplasty Reduces Monocyte Binding and Induces Apoptosis, Circulation 1999;100, pp. 1830-1835.

Odoux C. et al., Endothelin-1 secretion by alveolar macrophages in systemic sclerosis, Am. J. Respir. Crit. Care Med. 1997 Nov;156(5), pp. 1429-1435 (Abstract Only).

Ostensen M. et al., Nonsteroidal anti-inflammatory drugs in systemic lupus erythematosus, Lupus (2001) 10, pp. 135-139.

Piazza G.A. et al., Antineoplastic Drugs Sulindac Sulfide and Sulfone Inhibit Cell Growth by Inducing Apoptosis, Cancer Research 55, Jul 15 1995, pp. 3110-3116.

Reis E. et al., Sulindac inhibits neointimal formation after arterial injury in wild-type and apolipoprotein E-deficient mice, PNAS 97(23): pp. 12764-12769.

Rice P.L. et al., Inhibition of extracellular signal-regulated kinase 1/2 phosphorylation and induction of apoptosis by sulindac metabolites, Cancer Research 2001, Feb 15;61(4), pp. 1541-1547 (Abstract Only).

Soh, Jae-Won et al., Cyclic GMP Mediates Apoptosis Induced by Sulindac Derivatives via Activation of c-Jun NH<sub>2</sub>-Terminal Kinase 1, Clinical Cancer Research Vol. 6, pp. 4136-4141, October 2000.

Soh, Jae-Won et al., Protein Kinase G Activates the JNK1 Pathway via Phosphorylation of MEKK1, The Journal of Biological Chemistry, Vol. 276, No. 19, pp. 16406-16410 (2001).

Thompson, W.J. et al., Exisulind Induction of Apoptosis Involves Guanosine 3',5'-Cyclic Monophosphate Phosphodiesterase Inhibition, Protein Kinase G Activation, and Attenuated β-Catenin, Cancer Research 60, pp. 3338-3342, July 1, 2000.

Tien, Xiao-Ying, et al., Activation of the Cystic Fibrosis Transmembrane Conductance Regulator by cGMP in the Human Colonic Cancer Cell Line, Caco-2, The Journal of Biological Chemistry, Vol. 269, No. 1, pp. 51-54 (1994).

Tsukahara T et al., Cytophagic histiocytic panniculitis in systemic lupus erythematosus, Hiroshima J. Med. Sci., 1995 Mar; 44(1): 13-6 (Abstract Only).

Waddel W. R. et al., Sulindac for Polyposis of the Colon, The American Journal of Surgery, Vol. 157, Jan. 1989, pp. 175-179.

Waddel W. R. et al., Sulindac for Polyposis of the Colon, Journal of Surgical Oncology, 24: pp. 83-87 (1983).

Weyand CM and Goronzy JJ, HLA polymorphisms and T cells in rheumatoid arthritis, *Int. Rev. Immunol.* 1999; 19(1-2):37-39 (Abstract Only).

Wilder R.L. et al., Hormonal regulation of tumor necrosis factor-alpha, interleukin-12 and interleukin-10 production by activated macrophages. A disease-modifying mechanism in rheumatoid arthritis and systemic lupus erythematosus?, Ann. NY Acad. Sci 1999 June 22;876, pp. 14-31 (Abstract Only).

#### REMARKS

Applicants request that these references be made of record in this case, and that the Examiner indicate his review of these references by initialing and returning one copy of the PTO form enclosed.

This Information Disclosure Statement is being submitted before the mailing of the first Office Action on the merits pursuant to 37 C.F.R. § 1.97.

Respectfully submitted,



Robert W. Stevenson  
Reg. No. 31064  
Attorney for Applicants

Dated: September 5, 2001  
CELL PATHWAYS, INC.  
702 Electronic Drive  
Horsham, PA 19044  
(215) 706-3800

FORM PTO-1449		SERIAL NO. 09/938,009	CASE NO. P-188
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (use several sheets if necessary)		FILING DATE AUGUST 23, 2001	GROUP ART UNIT NOT YET ASSIGNED
		APPLICANT(S): WHITEHEAD ET AL.	

## REFERENCE DESIGNATION

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS/ SUBCLASS	FILING DATE
	A1	3,031,450	4/24/62	Fischer et al.		
	A2	3,161,654	12/15/64	Shen		
	A3	3,312,730	4/4/67	Winter et al.		
O I P E SEP 8 6 2001 PATENT & TRADEMARK OFFICE	A4	3,322,755	5/30/67	Roch et al.		
	A5	3,325,358	6/13/67	Winter et al.		
	A6	3,532,752	10/6/70	Shen		
	A7	3,642,785	2/15/72	Shen et al.		
	A8	3,647,858	3/7/72	Hinkley et al.		
	A9	3,654,349	4/4/72	Shen et al.		
	A10	3,692,651	9/19/72	Sletzingør et al.		
	A11	3,692,825	9/19/72	Conn		
	A12	3,737,455	6/5/73	Shen et al.		
	A13	3,851,063	11/26/74	Shen et al.		

## FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS/ SUBCLASS	TRANSLATION YES NO
	A14	EP 0 293 063 B1	3/18/92	EPO		
	A15	EP 0 347 146 B1	9/1/93	EPO		
	A16	EP 0 349 239 A2	1/3/90	EPO		
	A17	EP 0 352 960 B1	10/26/94	EPO		
	A18	EP 0 351 058 B1	6/2/93	EPO		

EXAMINER INITIAL	OTHER ART (Including Author, Title, Date, Pertinent Pages, etc.)	
	A19	Ahmad F. et al., IL-3 ad IL-4 Activate Cyclic Nucleotide Phosphodiesterases 3 (PDE3) and 4 (PDE4) by Different Mechanisms in FDCP2 Myeloid Cells, J. Immunology Vol. 162, Part 8, pp. 4864-4875 (Apr 15 1999).
	A20	Boven LA et al., Macrophage inflammatory protein-1 alpha (MIP-1alpha), MIP-1beta, and RANTES mRNA semiquantification and protein expression in active demyelinating multiple sclerosis (MS) lesions, Clin. Exp. Immunol. 2000 Nov.; 122(2): 257-63 (Abstract Only).
	A21	Cooper N. et al., A comparison of the inhibitory activity of PDE4 inhibitors on leukocyte PDE4 activity in vitro and eosinophil trafficking in vivo, British Journal of Pharmacology (1999) 126, pp. 1863-1871.
	A22	Czirjak L. et al., Investigation of the alveolar macrophages and T lymphocytes in 15 patients with systemic sclerosis, Clin Rheumatology 1999; 18(5), pp. 357-363 (Abstract Only).
	A23	Danahay H. et al., PDE4 inhibition and a corticosteroid in chronically antigen exposed conscious guinea-pigs, Clinical and Experimental Allergy, 1998, Vol. 28, pp. 513-522.
	A24	Duggan, D.E. et al., Identification of the Biologically Active Form of Sulindac, J. Pharm. & Exper. Therap., Vol. 201, No. 1, pp.8-13 (1977).

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449		SERIAL NO. 09/938,009	CASE NO. P-188
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (use several sheets if necessary)		FILING DATE AUGUST 23, 2001	GROUP ART UNIT NOT YET ASSIGNED
APPLICANT(S): WHITEHEAD ET AL.			

## REFERENCE DESIGNATION

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS/ SUBCLASS	FILING DATE
	A25 3,860,636	11/14/75	Shen et al.		
	A26 4,402,979	9/6/83	Shen et al.		
	A27 4,307,114	12/22/81	Dvornik et al.		
	A28 4,423,074	12/27/83	Dvornik et al.		
	A29 4,423,075	12/27/83	Dvornik et al.		
	A30 4,880,810	11/14/89	Lowe, III		
	A31 4,885,301	12/5/89	Coates		
	A32 5,298,525	3/29/94	Yoon et al.		
	A33 5,401,774	3/28/95	Pamukcu et al.		
	A34 5,470,873	11/28/95	Yoon		
	A35 5,488,055	1/30/96	Kumar et al.		
	A36 5,527,896	6/18/96	Wigler et al.		
	A37 5,602,019	2/11/97	Beavo et al.		

## FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	COUNTRY	CLASS/ SUBCLASS	TRANSLATION YES NO
	A38 EP 0 395 328 A2	10/31/90	EPO		
	A39 EP 0 428 268 A2	5/22/91	EPO		
	A40 EP 0 463 756 A1	1/2/92	EPO		
	A41 EP 0 526 004 A1	2/3/93	EPO		
	A42 EP 0 722 943 A1	1/8/96	EPO		

EXAMINER INITIAL	OTHER ART (Including Author, Title, Date, Pertinent Pages, etc.)	
	A43	Gantner F. et al., Characterization of the Phosphodiesterase (PDE) Pattern of in Vitro-Generated Human Dendritic Cells (DC) and the Influence of PDE Inhibitors on DC Function, Pulmonary Pharmacology & Therapeutics (1999) 12, pp. 377-386.
	A44	Gantner F. et al., In vitro differentiation of human monocytes to macrophages: change of PDE profile and its relationship to suppression of tumour necrosis factor- $\alpha$ release by PDE inhibitors, British Journal of Pharmacology (1997) 121, pp. 221-231.
	A45	Gehrman J. et al., Amyloid precursor protein (APP) expression in multiple sclerosis lesions, Glia 1995 Oct;15(2), pp. 141-151 (Abstract Only).
	A46	Germain N. et al., Selective phosphodiesterase inhibitors modulate the activity of alveolar macrophages from sensitized guinea-pigs, Eur. Respir. J. 1998;12, pp. 1334-1339.
	A47	Giembycz, M.A., Phosphodiesterase 4 Inhibitors and the Treatment of Asthma, Drugs 2000 Feb; 59(2), pp. 193-212.
	A48	Gonzaga, R.A.F. et al., The Lancet, 3/30/85, p. 751.

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449		SERIAL NO. 09/938,009	CASE NO. P-188
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (use several sheets if necessary)		FILING DATE AUGUST 23, 2001	GROUP ART UNIT NOT YET ASSIGNED
APPLICANT(S): WHITEHEAD ET AL.			

## REFERENCE DESIGNATION

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS/ SUBCLASS	FILING DATE
A49		5,602,171	2/11/97	Tang et al.		
A50		5,614,530	3/25/97	Kumar et al.		
A51		5,614,627	3/25/97	Takase et al.		
A52		5,708,022	1/13/98	Bastos et al.		
A53		5,776,752	7/7/98	Beavo et al.		
A54		5,789,553	8/4/98	Beavo et al.		
A55		5,798,374	8/25/98	Tang et al.		
A56		5,800,987	9/1/98	Beavo et al.		
A57		5,852,035	12/22/98	Pamukcu et al.		
A58		5,858,694	1/12/99	Piazza et al.		
A59		5,861,396	1/19/99	Niewöhner et al.		
A60		5,874,440	2/23/99	Pamukcu et al.		
A61		5,883,110	3/16/99	Tang et al.		

## FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS/ SUBCLASS	TRANSLATION YES NO
A62		EP 0 722 944 A1	1/8/96	EPO		
A63		EP 1 074 258 A3	4/18/01	EPO		
A64		GB 807,826	1/21/59	United Kingdom		
A65		GB 2 063 249 A	6/3/81	United Kingdom		
A66		HEI 8-311035	11/26/96	Japan		

EXAMINER INITIAL	OTHER ART (Including Author, Title, Date, Pertinent Pages, etc.)	
-	A67	Hammermann, R. et al., Phosphodiesterase Inhibitors and Forskolin Up-regulate Arginase Activity in Rabbit Alveolar Macrophages, Pulmonary Pharmacology and Therapeutics 2000; Vol. 13, No. 3, pp. 141-147.
	A68	He W. et al., Novel Cyclic Compounds as Potent Phosphodiesterase 4 Inhibitors, J. Med. Chem., Vol. 41, Part 22, pp. 4216-4223 (Oct 22 1998).
	A69	Hollander AP et al., Expression of hypoxia-inducible factor 1 alpha by macrophages in the rheumatoid synovium: implications for targeting of therapeutic genes to the inflamed joint, Arthritis Rheum. 2001 Jul; 44(7): 1540-4 (Abstract Only).
	A70	Imahashi K. et al., Type IV Phosphodiesterase Inhibitor Suppresses Insulin-Dependent Myocardial Glucose Uptake, Clin Exp Pharmacol Physiol 2001 Apr;28(4), pp. 290-291 (Abstract Only)
	A71	Ishikawa O. et al., Macrophage infiltration in the skin of patients with systemic sclerosis, J. Rheumatology 1992 Aug; 19(8), pp. 1202-1206 (Abstract Only).
	A72	Kapur S. et al., Expression of Nitric Oxide Synthase in Skeletal Muscle, Diabetes, Vol. 46, Nov. 1997, pp. 1691-1700.

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449		SERIAL NO. 09/938,009	CASE NO. P-188
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (use several sheets if necessary)		FILING DATE AUGUST 23, 2001	GROUP ART UNIT NOT YET ASSIGNED
		APPLICANT(S): WHITEHEAD ET AL.	

## REFERENCE DESIGNATION

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS/ SUBCLASS	FILING DATE
A73	5,885,834	3/23/99	Epstein		
A74	5,902,827	5/11/99	Pamukcu et al.		
A75	5,922,595	7/13/99	Fisher et al.		
A76	5,942,520	8/24/99	Pamukcu et al.		
A77	5,948,911	9/7/99	Pamukcu et al.		
A78	5,958,982	9/28/99	Pamukcu et al.		
A79	5,990,117	11/23/99	Pamukcu et al.		
A80	5,998,463	12/7/99	Hulin et al.		
A81	6,008,215	12/28/99	Flockerzi		
A82	6,015,677	1/18/00	Beavo et al.		
A83	6,034,099	3/7/00	Pamukcu et al.		
A84	6,037,345	3/14/00	Pamukcu et al.		
A85	6,046,199	4/4/00	Pamukcu et al.		

## FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	COUNTRY	CLASS/ SUBCLASS	TRANSLATION YES	TRANSLATION NO
A86	SHO 61-106521	5/24/86	Japan			
A87	WO 01/04099 A1	1/18/01	PCT			
A88	WO 00/12501	3/9/00	PCT			
A89	WO 00/26201	5/11/00	PCT			
A90	WO 00/23091	4/27/00	PCT			

EXAMINER INITIAL	OTHER ART (Including Author, Title, Date, Pertinent Pages, etc.)	
	A91	Kelly J. et al., Characterization of phosphodiesterase 4 in guinea-pig macrophages: multiple activities, association states and sensitivity to selective inhibitors, British Journal of Pharmacology (1998) 124, PP. 129-140.
	A92	Kelly J. et al., Phosphodiesterase 4 in macrophages: relationship between cAMP accumulation, suppression of cAMP hydrolysis and inhibition of [ <sup>3</sup> H]R-(–)-rolipram binding by selective inhibitors, Biochem. J. (1996) 318, pp. 425-436.
	A93	Kumar A. et al., Analgesic and anti-inflammatory effects of phosphodiesterase inhibitors, Indian J Exp Biol 2000 Jan;38(1), pp. 26-30 (Abstract Only)
	A94	Lee MS et al., A comparative immunohistochemical study of lichen planus and discoid lupus erythematosus, Australas J. Dermatol. 1996 Nov.; 37(4): 188-92 (Abstract Only).
	A95	McPherson M.A. et al., A cyclic nucleotide PDE5 inhibitor corrects defective mucin secretion in submandibular cells containing antibody directed against the cystic fibrosis transmembrane conductance regulator protein, FEBS Letters 464 (1999), pp. 48-52.
	A96	Mery P.F. et al., Erythro-9-(2-hydroxy-3-nonyl)adenine inhibits cyclic GMP-stimulated phosphodiesterase in isolated cardiac myocytes, Mol. Pharmacology 1995 Jul;48(1), pp. 121-130 (Abstract Only)

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449		SERIAL NO. 09/938,009	CASE NO. P-188
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (use several sheets if necessary)		FILING DATE AUGUST 23, 2001	GROUP ART UNIT NOT YET ASSIGNED
		APPLICANT(S): WHITEHEAD ET AL.	

## REFERENCE DESIGNATION

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS/ SUBCLASS	FILING DATE
	A97	6,046,206	4/4/00	Pamukcu et al.		
	A98	6,046,216	4/4/00	Piazza et al.		
	A99	6,060,477	5/9/00	Piazza et al.		
	A100	6,066,634	5/23/00	Sperl et al.		
<i>OIE SEP 6 2001 PATENT &amp; TRADEMARK OFFICE</i>						
	A101	6,069,240	5/30/00	Wigler et al.		
	A102	6,071,934	6/6/00	Sperl et al.		
	A103	6,077,842	6/20/00	Pamukcu et al.		
	A104	6,080,540	6/27/00	Wigler et al.		
	A105	6,080,742	6/27/00	Germann et al.		
	A106	6,080,772	6/27/00	Tang et al.		
	A107	6,100,025	8/8/00	Wigler et al.		
	A108	6,107,295	8/22/00	Rochus et al.		
	A109	6,124,303	9/26/00	Pamukcu et al.		

## FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS/ SUBCLASS	TRANSLATION YES NO
	A110	WO 00/26208	5/11/00	PCT		
	A111	WO 00/27861	5/18/00	PCT		
	A112	WO 00/42017	7/20/00	PCT		
	A113	WO 00/42018	7/20/00	PCT		
	A114	WO 00/42019	7/20/00	PCT		

EXAMINER INITIAL	OTHER ART (Including Author, Title, Date, Pertinent Pages, etc.)	
	A115	Méry, Pierre-François et al., EHNA as an Inhibitor of PDE2: A Pharmacological and Biochemical Study in Cardiac Myocytes, Phosphodiesterase Inhibitors (1996), pp. 81-88.
	A116	Michie, A.M. et al., Rapid regulation of PDE-2 and PDE-4 cyclic AMP phosphodiesterase activity following ligation of the T cell antigen receptor on thymocytes: analysis using the selective inhibitors erythro-9-(2-hydroxy-3-nonyl)-adenine (EHNA) and rolipram, Cell Signal 1996 Feb;8(2), pp. 97-110.
	A117	Niebauer J. et al., Local L-Arginine Delivery After Balloon Angioplasty Reduces Monocyte Binding and Induces Apoptosis, Circulation 1999;100, pp. 1830-1835.
	A118	Odoux C. et al., Endothelin-1 secretion by alveolar macrophages in systemic sclerosis, Am. J. Respir. Crit. Care Med. 1997 Nov;156(5), pp. 1429-1435 (Abstract Only).
	A119	Ostensen M. et al., Nonsteroidal anti-inflammatory drugs in systemic lupus erythematosus, Lupus (2001) 10, pp. 135-139.
	A120	Piazza G.A. et al., Antineoplastic Drugs Sulindac Sulfide and Sulfone Inhibit Cell Growth by Inducing Apoptosis, Cancer Research 55, Jul 15 1995, pp. 3110-3116.

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449		SERIAL NO. 09/938,009	CASE NO. P-188
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (use several sheets if necessary)		FILING DATE AUGUST 23, 2001	GROUP ART UNIT NOT YET ASSIGNED
		APPLICANT(S): WHITEHEAD ET AL.	

## REFERENCE DESIGNATION

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS/ SUBCLASS	FILING DATE
A121	6,133,271	10/17/00	Pamukcu et al.		
A122	6,143,746	11/7/00	Daugan et al.		
A123	6,143,759	11/7/00	Flockerzi		
A124	6,143,765	11/7/00	Tang et al.		
A125	6,143,777	11/7/00	Jonas et al.		
A126	6,169,090	1/2/01	Dyke et al.		
A127	6,174,884	1/16/01	Haning et al.		
A128	6,187,779	2/13/01	Pamukcu et al.		
A129	6,200,771	3/13/01	Liu et al.		
A130	6,200,980	3/13/01	Piazza et al.		
A131	6,207,666	3/27/01	Piazza et al.		
A132	6,211,177	4/3/01	Sperl et al.		
A133	6,211,220	4/3/01	Pamukcu et al.		

## FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	COUNTRY	CLASS/ SUBCLASS	TRANSLATION YES NO
A134	WO 00/42034	7/20/00	PCT		
A135	WO 00/59890	10/12/00	PCT		
A136	WO 00/64424	11/2/00	PCT		
A137	WO 99/65880	11/23/99	PCT		
A138	WO 98/19679A1	5/14/98	PCT (Claims Only)		

EXAMINER INITIAL	OTHER ART (Including Author, Title, Date, Pertinent Pages, etc.)	
	A139	Reis E. et al., Sulindac inhibits neointimal formation after arterial injury in wild-type and apolipoprotein E-deficient mice, PNAS 97(23): pp. 12764-12769.
	A140	Rice P.L. et al., Inhibition of extracellular signal-regulated kinase 1/2 phosphorylation and induction of apoptosis by sulindac metabolites, Cancer Research 2001, Feb 15;61(4), pp. 1541-1547 (Abstract Only).
	A141	Soh, Jae-Won et al., Cyclic GMP Mediates Apoptosis Induced by Sulindac Derivatives via Activation of c-Jun NH <sub>2</sub> -Terminal Kinase 1, Clinical Cancer Research Vol. 6, pp. 4136-4141, October 2000.
	A142	Soh, Jae-Won et al., Protein Kinase G Activates the JNK1 Pathway via Phosphorylation of MEKK1, The Journal of Biological Chemistry, Vol. 276, No. 19, pp. 16406-16410 (2001).
	A143	Thompson, W.J. et al., Exisulind Induction of Apoptosis Involves Guanosine 3',5'-Cyclic Monophosphate Phosphodiesterase Inhibition, Protein Kinase G Activation, and Attenuated $\beta$ -Catenin, Cancer Research 60, pp. 3338-3342, July 1, 2000.
	A144	Tien, Xiao-Ying, et al., Activation of the Cystic Fibrosis Transmembrane Conductance Regulator by cGMP in the Human Colonic Cancer Cell Line, Caco-2, The Journal of Biological Chemistry, Vol. 269, No. 1, pp. 51-54 (1994).

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449	SERIAL NO. 09/938,009	CASE NO. P-188
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (use several sheets if necessary)		FILING DATE AUGUST 23, 2001
GROUP ART UNIT NOT YET ASSIGNED		
APPLICANT(S): WHITEHEAD ET AL.		

## **REFERENCE DESIGNATION**

## **U.S. PATENT DOCUMENTS.**



## FOREIGN PATENT DOCUMENTS

FOREIGN PATENT DOCUMENT						
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS/ SUBCLASS	TRANSLATION YES NO
	A155	WO 98/17668	4/30/98	PCT		
	A156	WO 98/14448	4/9/98	PCT		
	A157	WO 98/06722	2/19/98	PCT		
	A158	WO 97/24334	7/10/97	PCT		
	A159	WO 97/03985	2/6/97	PCT		

EXAMINER INITIAL	OTHER ART (Including Author, Title, Date, Pertinent Pages, etc.)	
	A160	Tsukahara T et al., Cytophagic histiocytic panniculitis in systemic lupus erythematosus, <i>Hiroshima J. Med. Sci.</i> , 1995 Mar; 44(1): 13-6 (Abstract Only).
	A161	Waddel W. R. et al., Sulindac for Polyposis of the Colon, <i>The American Journal of Surgery</i> , Vol. 157, Jan. 1989, pp. 175-179.
	A162	Waddel W. R. et al., Sulindac for Polyposis of the Colon, <i>Journal of Surgical Oncology</i> , 24: pp. 83-87 (1983).
	A163	Weyand CM and Goronzy JJ, HLA polymorphisms and T cells in rheumatoid arthritis, <i>Int. Rev. Immunol.</i> 1999; 19(1-2):37-39 (Abstract Only).
	A164	Wilder R.L. et al., Hormonal regulation of tumor necrosis factor-alpha, interleukin-12 and interleukin-10 production by activated macrophages. A disease-modifying mechanism in rheumatoid arthritis and systemic lupus erythematosus?, <i>Ann. NY Acad. Sci</i> 1999 June 22;876, pp. 14-31 (Abstract Only).

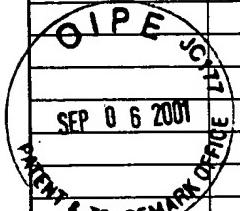
EXAMINER	DATE CONSIDERED
----------	-----------------

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449	SERIAL NO. 09/938,009	CASE NO. P-188
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (use several sheets if necessary)		FILING DATE AUGUST 23, 2001
APPLICANT(S): WHITEHEAD ET AL.		

## **REFERENCE DESIGNATION**

## U.S. PATENT DOCUMENTS



## FOREIGN PATENT DOCUMENTS

FOREIGN PATENT DOCUMENTS						
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS/ SUBCLASS	TRANSLATION YES NO
	A165	WO 97/03675	2/6/97	PCT		
	A166	WO 94/29277	11/22/94	PCT		
	A167	WO 93/07149	4/15/93	PCT		

EXAMINER	DATE CONSIDERED
----------	-----------------

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609;  
Draw line through citation if not in conformance and not considered. Include copy of this form with next  
communication to applicant.